Online Resources

Online Resource S1: CONSORT 2010 Checklist

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	P1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	P1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	P1-3
	2b	Specific objectives or hypotheses	P3
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	P4-6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	P4
	4b	Settings and locations where the data were collected	P4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	P6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	P5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	P5-6
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA

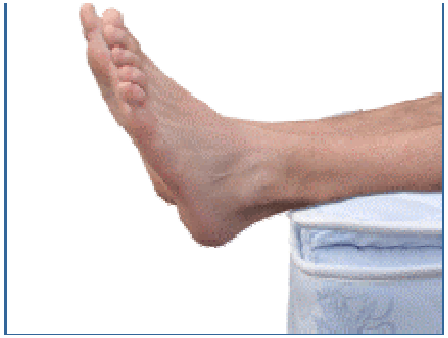
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	P6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	P6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	P6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	P6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	P6
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	P7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	P7
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	P5-6
	13b	For each group, losses and exclusions after randomisation, together with reasons	P5-6
Recruitment	14a	Dates defining the periods of recruitment and follow-up	P5-6
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Figure 2
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 2
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Figure 3

Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	P10
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	P10
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	P9
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	P9
Other information			
Registration	23	Registration number and name of trial registry	P11
Protocol	24	Where the full trial protocol can be accessed, if available	P11
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	P11

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Online Resource S2: New Sleeping Position

THE NEW SLEEPING POSITION



The new sleeping position requires you to reposition yourself in your bed when lying on your back so that your feet (and ankles) hang over the end of the mattress, i.e. off the end of the bed (please see the picture). When using this new sleeping position, you will need to use a blanket (or two) to cover your feet to keep them warm. It is best to tuck one end of the blanket under the mattress (under foot end) and then wrap the other end of the blanket over the quilt or bed- covers you are using.

If you share your bed with your partner/spouse it is likely that you will both need to use single quilt as it will be difficult to share a double quilt if you are lying further down the bed (so that your feet can hang over the end of the mattress). Don't worry if you move from this position during the night, i.e. turn onto your side. The key thing is to try and adopt the new sleeping position for the periods that you are lying on your back.

You may find that it takes a little bit of time getting used to lying in this new position but once you have got used to it, it soon feels quite normal. If you cannot get used to the new sleeping position, please inform Dr Bhattacharjee.

The new sleeping position is aimed at preventing the knee being 'pushed' into full extension (straight) when you are lying on your back. It is hoped that this position will be beneficial to your knees.

We request that you maintain this new sleeping position for three months. During this time we will ask you to complete the pain/discomfort questionnaire again at one and three months following changing to the new sleeping position.

If you have any problem please telephone 01274 ****** to speak to Dr Bhattacharjee at any time. In his absence, please leave a message so that he can get back to you.

Online Resource S3: Study Protocol

This document contains an overview of the proposed study, including rationale and protocol etc. that was submitted in obtaining ethics approval to conduct the study.

This protocol has regard for the HRA guidance

Version 1.0; 9th January 2018

IRAS Number:

Sponsor: University of Bradford

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.
I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor
I also confirm that I will make the findings of the trial publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

Chief Investigator:

Signature: 

Date:
11/01/2018

Name: (please print): Dr John Buckley

1.0 Trial Summary

Trial Title	Reducing knee compression loading when sleeping supine: benefits in patients with knee osteoarthritis	
short title	Reducing knee compression when sleeping in those with knee OA	
Clinical Phase		
Trial Design	'Proof of concept': undertaken as small randomised control trial (comparable to a Phase I trial)	
Trial Participants	Those with confirmed knee OA	
Planned Sample Size	46	
Treatment	Self-administered change in sleeping position	
Follow up	Assessment at 1 and 3 month post change in sleeping position	
Planned Trial Period	4-months (each participant)	
	Objectives	*Outcome Measures*
Primary	Change in sleeping position provides pain relief	KOOS Pain score
Secondary	Change in sleeping position provides symptom improvement	KOOS knee-symptoms and physical function scores

2.0 Overview of study

2.1 Aim: The aim is to determine whether a change in sleeping position so as to prevent the knee being 'pushed' into full extension when lying supine provides pain relief and symptom improvement in individuals with knee-OA.

2.1.1 Hypothesis: Sleeping with feet hanging off end of mattress will provide pain relief and symptom improvement in those with knee-OA.

2.2 Background

Increased bodyweight or limb malalignment, causing supra-physiological knee compression has been shown to produce degenerative changes in rat knee joint cartilage, including a decrease in cartilage modulus and thickness and an increase in matrix loss (Roemhildt et al., 2013: Osteoarthr. Cartil., 21, 346-357). Additionally, fifty minutes of isometric loading has been shown, in the rabbit knee, to lead to the death of cells (chondrocytes) that produce and maintain cartilage matrix (Horisberger et al., 2013: Clin. Biomech., 28, 536-543). Both of these features have been shown to be risk factors in the onset and progression of osteoarthritis (Setton et al., 1999: Osteoarthr. Cart., 7, 2-14; Pritzker et al., 2006: Osteoarthr. Carti., 14, 13-29). We have recently completed an experimental study in healthy participants (Buckley et al., 2018: J. Musculoskelet. Disord. Treat., 4, 1-5) that demonstrated that when lying supine, as the heel protrudes 'outwards' from the back of the leg, contact forces from the heel 'push' the knee into full extension, and the resulting knee-extension moment is comparable to that when standing. Furthermore, this moment increases further if the feet are elevated above the hips, as might occur when lying on a 'soft' or sunken mattress. This suggests that prolonged knee compression loading as might occur when sleeping supine may be large enough to have detrimental effects on knee cartilage, and thus such prolonged knee compression loading may be related to the onset of knee pain and hence to osteoarthritis onset and progression. When lying supine the feet naturally turn outwards (encouraged by the weight of the blankets or quilt) which will mean compression within the knee will be higher on the medial aspect, which is where knee OA commonly occurs in human knees.

Individuals with knee OA experience chronic knee pain with related decrease in mobility, which impacts upon their quality of life. In an attempt to alleviate knee pain and discomfort they experience, those suffering knee-OA and/or chronic knee pain, place wedged cushioning under the knees when in bed, however, this is ineffective because the cushion becomes displaced when a person moves during sleep. In our recent study (Buckley et al., in review) we demonstrated that lying with the heels 'hanging off' the end of the support eliminates the tendency for an external knee-extension moment being applied and this occurred even if the hips were at a lower height than the feet as might happen when sleeping on soft or sunken mattress. This suggests that lying with the heels hanging over the end of a standard mattress or on a mattress that is sloped or 'stepped' downwards at the 'foot end', which will reduce the compression experienced at the knee to zero, may help reduce knee pain and provide symptom improvement. The lead applicant has recently shown in a handful of volunteers with chronic knee pain (n=3), that

using this sleeping position (lying on back with feet hanging over end of mattress) lead to a reduction in knee-pain and improvement in associated symptoms. Specifically, KOOS pain and functional ability scores improved following a change in sleeping position (by 14 and 12 percentage points respectively. Such improvements represent meaningful changes, and was reflected by an improvement in quality of life assessment scores. The aim of the proposed study is to determine whether this simple intervention could have similar benefits in those with confirmed knee-OA.

2.3 Rationale

Previous work has shown that sustained (concentric) knee loading causes degenerative changes (wearing) of the joint linings (cartilage) at the end of and between the bones of the knee. Such degenerative wearing is associated with chronic knee pain and accompanying reduced mobility. There are several previous studies that have shown interventions to reduce knee loading during standing and walking can alleviate knee-pain and slow the progression of knee osteoarthritis. There are no studies that have directly investigating whether reducing the magnitude of the knee compression loading experienced when laying on one's back will lead to a reduction in knee-pain and associated symptoms. If the proposed intervention proves effective in individuals with knee-OA by inducing pain relief and symptom improvement, this will highlight that this simple, cheap and safe intervention has the potential to be widely used by individuals suffering with knee-OA and/or those with chronic knee pain. If it proves effective it would also suggest that this simple intervention may slow osteoarthritis progression and hence delay knee replacement surgery, and thus could have an important and beneficial impact on the quality of life for the many individual suffering with knee-OA.

2.4 Assessment and management of risk

It is possible that some patients find it difficult to be comfortable lying supine with their feet hanging over the end of the mattress and/or after adopting such a sleeping position experience a worsening of knee pain. The 'Information sheet' will outline that should either of the above scenarios occur participants should revert back to the way they used to lie on their back when sleeping prior to involvement in the study.

When lying supine with feet hanging over end of mattress, it may be difficult to keep the feet warm. Participants in the 'intervention group' will be given instruction on how to use a blanket to cover their feet to keep them warm (when they are hanging over end of mattress). They will also be informed that if they share their bed with partner/spouse it is likely that they will both need to use single quilts as it would be difficult sharing a quilt if they are lying further down the bed than their partner/spouse.

- **2.5 Programme and Methodology**

2.5.1 Research design: Small clinical trial (comparable to a Phase I trial)

2.5.2 Participant identification and Recruitment

Based on formal sample size calculation, the estimated sample size for two-sample comparison of means, with power=0.90, alpha=0.05; indicates we need to recruit two groups (intervention, control) each of 49 participants. This is based on a typical mean KOOS pain-score (primary outcome measure) for elderly with knee-OA of 55.5 ± 21.9 and a change in pain-score of at least 14.3, which is thought to represent a true and meaningful change for elderly individuals (Collins et al., 2016: Osteoarthr. Cart. 24, 1317-1329). To guard against participants 'dropping out', we will aim to recruit 98 participants in total. Participants will be recruited from patients at Idle Medical Centre (Bradford, West Yorkshire). Potential study participants will be those with confirmed knee-OA and/or with chronic knee pain and associated dysfunction. Posters/leaflets displayed in Idle Medical Centre, will be used to highlight that if such individuals wish to take part in a research study about chronic knee pain they should make an appointment to see Dr Bhattacharjee.

2.5.2.1 Inclusion/exclusion criteria

Those indicating they would be willing to consider participating in the study will have the purpose of the study and what is involved in participating in it, explained by Dr Bhattacharjee. Those with chronic knee pain will be sent for x-ray as part of their 'usual care'. All patients with knee-OA (equivalent to at least grade II on KL scale) will be invited to take part. Dr Bhattacharjee will also confirm/clarify whether they usually/frequently lay on their back when sleeping. They will also be given a Participant Information sheet that explains the aim of the study and what participation in it involves. Those with the following will be excluded: rheumatoid arthritis; chronic cardiopulmonary problems; lower-limb joint(or joint surface) replacement and/or previous knee surgery within previous 12 months; unable to lie supine in bed (medical reason); pregnancy; diagnosed with inflammatory arthropathy; peripheral neuropathy or other sensory problems; steroid injection in the knee within previous 3 months; under 18 years of age; unable to give consent due to lack of mental capacity; currently involved in any research study related to knee OA; those without knee OA.

2.5.3 Protocol and intervention

Following giving their consent to take part, participants will asked to complete a questionnaire asking about the pain and/or discomfort they are currently experiencing (the Knee Injury and Osteoarthritis Outcome Score, KOOS). Participants will be asked to complete the questionnaire for a second time one month later, and once they have completed it participants will be randomly assigned to either an intervention group or a control group. Randomisation will be undertaken using the allocation concealment approach ('sealed envelope').

On the day participants complete the questionnaire a second time, those assigned to the intervention group will be asked to henceforth adopt the new sleeping position, whereas those in the control group will be asked to maintain their normal sleeping position. Those in the intervention group will be provided details about the new sleeping position and given opportunity to ask question about it. They

will be asked to adopt the new sleeping position for 3 months during which they will be asked to again complete the questionnaire 1 and 3 months after changing sleeping position. The control group will complete the questionnaires at the same time intervals as the intervention group. If the study shows that the new sleeping position is beneficial, then those in the control group will be told about the new sleeping position at the end of the study.

Questionnaires will be given to participants by Dr Bhattacharjee, and participants will be asked to complete the questionnaires and to return them (via stamped address envelop) to the lead applicant at University of Bradford. The KOOS questionnaire has been validated and widely used to access knee pain and functioning in those with knee-OA.

The Information Sheet will indicate that at the end of the participant's involvement in the study, it will be up to the participant to decide if they wish to revert back to lying on their mattress in the way they used to do prior to participation in this study. The Information Sheet will also highlight that Dr Bhattacharjee will be responsible for their care during their time in the study.

2.5.4 Outcome measure and analysis

The outcomes assessed will be the KOOS scores of knee pain (primary), and knee-symptoms and physical function (secondary). The hypothesis is that a change in sleeping position will lead to improvements in these scores after 1 and/or 3 months of using the new sleeping position. To test this hypothesis, the KOOS scores collected of the intervention group following changing to the new sleeping position will be compared to KOOS scores collected prior to changing to the new sleeping position. KOOS scores collected of the control group (at same time points as the intervention group) will be analysed to check for any placebo effects. Our plan is to use a mixed-mode linear model to look at differences pre and post changing to new sleeping position, and between groups at equivalent time points to control/account for any placebo effects. Statistical analyses will be undertaken at the University of Bradford by Mr Andy Scally (medical statistician).

2.5.5 Access and Storage of personal and study data

Patient medical records and contact details will only be seen by Dr Bhattacharjee. Reviewing of records is common practice during any consultation. Patient records will not be reviewed by anyone else, and thus there is no potential for breach of any duty of confidentiality.

The questionnaires participants will be asked to complete will include a participant identification number and thus questionnaire responses will be anonymous, i.e. they will not include patient names only an identification number. The anonymised questionnaire data, which will be analysed by lead applicant at University of Bradford, will be stored (on his password protected pc) for 5 years and then destroyed.

2.5.6 Research management

This is a relatively small-scale study which is about assessing the efficacy of a simple, and self-administered, intervention. As such the management of the research is relatively straight forward. Doctor Bhattacharjee (at Idle Medical Centre) will be responsible for participant recruitment; including doing eligibility/screening checks; explaining the study to potential participants; and gaining consent. He will also be responsible for assigning participant identification numbers and then sending or giving out the 4 sets of questionnaires to each participant (over 4 month period). The lead applicant will be responsible for overseeing the questionnaire data input and preliminary analysis; and making any 'first drafts' regarding dissemination of findings.

The lead applicant's expertise is in clinical biomechanics and he has a track record in conducting lab-based experimental studies in clinical populations, including small control trials. He has recently completed (either as PI or CI) research projects supported by EPSRC, BBSRC and NIHR.

Dr Bhattacharjee is a full time GP Partner with clinical, administrative, managerial and teaching roles. He has GPwSI special interest in musculoskeletal, joint injection, and minor surgery. He has previously completed a double-blinded prospective study on 'Use of combination of Lignocaine and Bupivacaine in haematoma block'.

3.0 Dissemination

Although dissemination of findings via high-quality journals and presentation at international conference represents the main dissemination strategy, results will also be disseminated to 'end-users'. This will be achieved by conversing with patient groups at Idle Medical Centre and/or by submitting articles to popular professional periodicals such as Centre and/or NHS Newsletters.

4.0 Project management

As a relatively small and simple study project management will be undertaken by the PI and CI themselves.

5.0 References

- Roemhildt M.L., Beynnon B.D., Gauthier A.E., Gardner-Morse M., Ertemy F., Badger G.J. (2013) Chronic in vivo load alteration induces degenerative changes in the rat tibiofemoral joint. Osteoarthr. Cart.; 21: 346-57.
- Horisberger M., Fortuna R., Valderrabano V., Herzog W. (2013) Long-term repetitive mechanical loading of the knee joint by in vivo muscle stimulation accelerates cartilage degeneration and increases chondrocyte death in a rabbit model. Clin. Biomech.; 28: 536-43.

- Setton L.A., Elliott D.M., Mow V.C. (1999) Altered mechanics of cartilage with osteoarthritis: human osteoarthritis and an experimental model of joint degeneration. Osteoarthr. Cart.; 7: 2-14.
- Pritzker K.P.H., Gay S., Jimenez S.A., Ostergaard K., Pelletier J.P., Revell P.A., et al. Osteoarthritis cartilage histopathology: grading and staging. Osteoarthr. Cart. 2006; 14:13-29.
- Buckley J.G., Nichols S.Bhattacharjee C. (2018) Knee compression loading when lying supine: effects of foot position on mattress. J. Musculoskelet. Disord. Treat.; 4, 1-5.
- Collins N.J., Prinsen C.A., Christensen R.; Bartels E.M., Terwee C.B. Roos E.M. (2016) Knee Injury and Osteoarthritis Outcome Score (KOOS): systematic review and meta-analysis of measurement properties. Osteoarthr. Cartil.; 24, 1317-1329.